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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,328	05/15/2002	Jay M. Meythaler	UAB-15452/22	3601

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EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 05/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,328	MEYTHALER ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-13,15-18 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-13,15-18 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 22, 2006 has been entered.

Claims 1-3, 5-13, 15-18 and 26 are pending in this application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 5-13, 15-18 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aebisher et al. U.S. Patent No. 5,474,547 A and Bergmann, Clinical Neuropharmacology 1985 (IDS from 1/14/04 document AB).

Aebisher et al. teach a method of alleviation of movement disorders associated with Parkinson's disease, Huntington's disease and epilepsy comprising administering GABA, GABA prodrugs and GABA potentiators via implantation of devices which would release said neuroinhibitory compounds into the brain (column 3, lines 40-67).

Aebisher et al. does not teach specifically the spastic disorders of claims 7, 8 and 26 such as spastic dystonia, spastic hypertonia, spastic disorders caused by traumatic brain injury, and idiopathic dystonia, or torsional dystonia, however, the disorders cited in Aebisher et al. such as epilepsy and Parkinson's disease are well known disorders marked by spasticity and convulsions as in the instantly claimed disorders.

Thus, it would have been made obvious to one of ordinary skill in art at the time the invention was made to treat spastic dystonia, spastic hypertonia, spastic disorders caused by traumatic brain injury, and idiopathic dystonia, or torsional dystonia with gamma-amino-butyramide motivated by the teachings of Aebisher et al. who teach administration of GABA, GABA prodrugs and GABA potentiators for treatment of disorders of spasticity such as Parkinson's and epilepsy.

Aebisher et al. does not specifically teach Gamma aminobutyramide.

Bergmann teaches that Progabide, a prodrug of GABA is metabolized to α chloro-4'phenyl fluoro-5 hydroxy-2-benzylidene amino 4 butanoate sodium, and then to **GABAmide** (gamma aminobutyramide) which appears in the circulation and in the brain

in a few minutes after administration (see pages 13-14). The compound is employed to treat spasticity (page 19) epilepsy and convulsions (pages 17-19) and Parkinson's disease (spastic hypertonia) (pages 20-21). Although it is not specifically recited, GABAmide is necessarily present because of the administration of progabide for the treatment of seizure disorders,and the inevitable metabolism of progabide to GABAmide as stated above.

Regarding claims 2, 3, 5, 6, 13, 15, 16 and 17 drawn to intrathecal administration, intraventricular administration, by an implantable pump and a spinal catheter for delivery of gamma aminobutyramide, Aebisher et al. teach an implantable pump for administration of GABA and its prodrugs and potentiators. Bergmann teaches that Progabide, a prodrug of GABA is metabolized **GABAmide** (gamma aminobutyramide), and it appears in the circulation and in the brain in a few minutes after administration (see pages 13-14). Thus would have been made obvious to one of ordinary skill in art at the time it was made to administer prodrugs/derivatives of gamma aminobutyramide intrathecally, intraventricularly, by an implantable pump or spinal catheter motivated by the teaching of Aebisher et al. who administers GABA by an implantable pump in the brain and the teaching of Bergmann that gastric-resistant formulations of progabide have been shown to result in incomplete absorption and lower serum levels. As anyone of ordinary skill in the art will appreciate modes of administration are art-recognized result-effective variables and it would have been obvious to one of ordinary skill in the art to optimize them from the teachings of the prior art. Since the gastric-resistant formulations result in incomplete absorption, it would

have been obvious to administer the compound by parenteral means, such as intraventricularly and intrathecally. Further evidence of obviousness would flow from the teaching of Aebisher et al. who teach administration of GABA by an implantable pump in the brain wherein the GABA, GABA prodrugs or GABA potentiators would metabolize to GABAmide in the ventricles of the brain, this resulting in intraventricular administration. Regarding the intrathecal administration, intrathecal administration means administering parenterally to the subarachnoid space. The subarachnoid space is the compartment within the spinal column that contains the cerebrospinal fluid (CSF). CSF is produced in the ventricular system of the brain. It communicates freely with the subarachnoid space via the foramina of Luschka and Magendie near the brainstem. Thus would have been made obvious to one of ordinary skill in art at the time it was made to administer prodrugs/derivatives of gamma aminobutyramide intrathecally, intraventricularly, by an implantable pump or spinal catheter motivated by the teaching of Aebisher et al. who administers GABA by an implantable pump in the brain and the teaching of Bergmann that gastric-resistant formulations of progabide have been shown to result in incomplete absorption and lower serum levels. Since the gastric-resistant formulations result in incomplete absorption, it would have been obvious to administer the compound by parenteral means, such as intraventricularly and intrathecally since all would result in CSF administration as in Aebisher et al.

Response to Arguments

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that the claimed invention overcomes the principal cause of side effects associated with progabide by delivering a metabolite thereof without the aromatic by product 4-chlorophenyl-5-fluoro-2-hydroxyphenylmethanone) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Regarding the assertion that GABAmide is sufficiently stable as to be amenable to intrathecal and intraventricular delivery, applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections. The claim language *comprising* leaves the claim open for the inclusion of unspecified ingredients, even in major amounts, thus, it does not exclude the GABA, GABA prodrugs and GABA potentiators of Aebisher et al. and the Progabide, which metabolizes to α chloro-4'phenyl fluoro-5 hydroxy-2-benzylidene amino 4 butanoate sodium, and then to **GABAmide** (gamma aminobutyramide) of Bergmann.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies

(i.e., GABAmide is not taught to act like progabide, SL 75012 or GABA at all known GABA receptor sites) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Regarding applicants assertion that the unexpected reduction in side effects associated with GABAmide administration because of the 4-chlorophenyl-5-fluoro-2-hydroxyphenylmethanone byproduct, this allegation cannot be found in applicant's specification.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Donna Jagoe
Patent Examiner
Art Unit 1614

May 11, 2006

Ardin H. Marschel 5/15/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER